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IV. 8. Cerebral Circulatory and Metabolic Changes Following Vascular Reconstruction in Cerebral Occlusive Disease

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Introduction

Ever since the report of results of international cooperative study on extracranial-intracranial bypass (EC-IC) in 1985,[16,17] there have been many debates[1,3,8,14,15] on the indication for and effectiveness of such surgical therapy in cases of ischemic cerebrovascular disease. We have made a study of the changes in cerebral circulation and metabolism in the chronic period following vascular reconstruction in such patients using positron emission tomography (PET). Here we discuss those results and related issues.

Materials and Method

Patients

Twelve patients with cerebrovascular occlusive disease were studied with PET before and after vascular reconstruction between August 1984 and December 1989. Ages ranged from 41 to 67 (mean 57.3); eleven were male and one was female (Table 1). The patients were admitted to hospital for attacks of cerebral ischemia, the nature of which was TIA in two cases, RIND in one case, minor completed stroke in eight cases, and vertebrobasilar insufficiency in one case. In cerebral angiograms, the responsible lesion was thought to be occlusion of the internal carotid artery (ICA) in three cases, stenosis of the ICA in two cases, stenosis of the basilar artery (BA) in three cases, bilateral stenosis of the vertebral arteries (VA) in three cases, and bilateral occlusion of the VA in one case. The surgery was thromboendarterectomy of the ICA in one case and superficial temporal artery to middle cerebral artery (STA-MCA) anastomosis in four cases, all of which had anastomosis to the proximal M2 region,[4] for those with lesions of the ICA. For the seven cases with lesions of the vertebro-basilar system, STA-superior cerebellar artery (SCA) anastomosis was performed in five cases and VA transposition was done in two cases.

Indication for surgery was decided when the following conditions were satisfied; 1) stroke attacks were TIA, RIND or minor completed stroke, and preoperative symptoms were none or mild, 2) a vascular lesion seen angiographically was thought to be responsible for the symptoms, and hemodynamic mechanism was suspected for occurrence of the symptoms, 3) the possibility of embolism due to cardiac disease or others could be ruled out. The surgery was undertaken at least one month following the last attack of cerebral ischemia.

Scanner and Procedure

In the PET study, ECAT II (EG&G, Ortec) and PT-931 (CTI, Knoxville, Tennessee) were used. The spatial resolutions were 17mm and 8mm in Full Width Half Maximum (FWHM) in ECAT II and PT-931, and slice thickness were 18mm and 7mm respectively. Regional cerebral blood flow(CBF), oxygen extraction fraction (OEF) and cerebral metabolic rate of oxygen ($CMRO_2$) were measured with the continuous inhalation method[5)] of $C^{15}O_2$, $^{15}O_2$ and $C^{15}O$ while the patients were at rest with eyes closed. The PET images were reconstructed using measured attenuation correction.

For the cases with ICA lesions, the regions of interest (ROIs) were the area of perfusion of the anterior cerebral artery (ACA), that of the MCA, the anterior watershed zone (AW) between the ACA and MCA regions, the area of perfusion of the posterior cerebral artery (PCA), and the posterior watershed area (PW) between the PCA and MCA regions. Measurements were taken both on the operated side and contralaterally. In addition, in the patients with lesions of the vertebro-basilar system, subtentorial measurements were also taken from a regions covering both cerebellar hemispheres.

Results

The pre-and postoperative values for the CBF, OEF and $CMRO_2$ of the various regions in the five cases of ICA lesions are shown in Figure 1, expressed as percentages of the preoperative values. There was a tendency for increases in the regions of perfusion (ACA and AW) contralaterally, as well as increases in the regions of perfusion of the MCA and ACA (MCA, ACA, AW and PW) on the operated side. There was a marked decrease in the OEF of the region of perfusion of the ACA and MCA on the operated side. Notable changes in $CMRO_2$ were not seen.

The mean CBF values in the ICA region showed significant increases from 28.1±4.59 to 35.2±5.35 ml/100g/min ($p<0.01$) and that of OEF revealed significant decrease from 0.53±0.10 to 0.43±0.07 ($p<0.01$) after the vascular reconstruction (Fig. 2). The control value of CBF, OEF and $CMRO_2$ in the cerebral cortex obtained from seven normal volunteer (age ranged from 52 to 71, with the mean age of 62) were 44.2±4.2 ml/100g/min, 0.46±0.04 and 3.13±0.58 ml/100g/min respectively.[9,10]

Percentage changes in CBF, OEF and $CMRO_2$ for the seven cases with lesions of the vertebro-basilar systems are shown in Fig. 3. A tendency for increases in CBF and decreases in OEF were seen over the entire brain, not only in the cerebellum and region of perfusion of the PCA. Although there were local variations, there was, overall, a mild increase in $CMRO_2$.

The mean CBF values in the both cerebellum showed significant increase from 32.1±6.09 to 37.7±9.22 ml/100g/min ($p<0.01$), and OEF showed also significant decrease from 0.54±0.08 to 0.48±0.09 ($p<0.01$). On the other hand, $CMRO_2$ disclosed a nonsignificant trend toward increase (Fig. 4).

On the basis of these data, the cases were divided into groups with preoperative mean OEF values above or below 0.55. The ROIs over the ICA and VBA showed that the preoperative CBF was significantly lower in the group with high OEF values preoperatively (28.5±5.37 ml/100g/min) as compared to that of in low OEF group (34.3±6.19 ml/100g/min), while postoperatively there was significant improvement in both CBF (37.5±10.2 ml/100g/min) and OEF (from 0.60±0.07 to 0.50±0.08)($p<0.01$). In contrast, in the group with low OEF values, although there was again a significant increase in CBF (39.9±8.05 ml/100g/min, $p<0.05$), the fall in OEF was not statistically significant. In both groups, there was a nonsignificant trend toward increasing $CMRO_2$ values (Fig. 5).

Discussion

There have already been many reports concerning the PET evaluation of vascular reconstruction performed in the chronic period following ischemic cerebrovascular attacks and concerning the use of various parameters in deciding on the indication for such surgery. Notable among such studies are the report by Baron et al.[2] on the evaluation of miserly perfusion by means of CBF, OEF and $CMRO_2$, the introduction of regional cerebral blood volume (CBV) and the calculation of regional cerebral perfusion pressure (CPP) either as CBV/CBF or CBF/CBV by Powers et al.[12,13] and Gibbs et al.[6,7] Noteworthy also is the evaluation of regional glucose metabolism (CMRGlu), CMRGlu/CBF and $CMRO_2$/CMRGlu by Leblanc et al.[11] Among these studies, it has been noted that CBF, OEF and CPP (CBV/CBF or CBF/CBV) are particularly effective in evaluating the pre- and postoperative cerebral hemodynamics. Specially in cases of surgical vascular reconstruction in which bypass to a site peripheral from the vascular occlusion is done, as in our cases, it was found that regional CPP is the most appropriate parameter.

All of the cases in the present series met the above-mentioned criteria for indication for surgery and the study was confined to those showing so-called "misery perfusion",[2] that is, decreased CBF and increased OEF in the region of what was thought to be the responsible vascular lesion. In the five cases with lesions of the ICA, there were postoperative increases in CBF and decreases in OEF over the region of perfusion of the ICA on the operated side. Similar findings were found contralaterally, principally over the region of perfusion of the ACA. Among the seven cases with VBA lesions, there were significant postoperative increases in CBF and decreases in OEF over the cerebellar hemisphere. This tendency was found not only over the cerebellum, but over the cerebrum as well. In addition to the fact that significant improvements were found in the area of misery perfusion on the operated side in each group, there is the suggestion that there were improvements in hemodynamics at other sites due to a decrease in the supply of blood through collateral pathways from these regions.

OEF is generally thought to vary in proportion to the oxygen demand to tissues and to correspond with the volume of regional cerebral blood flow, but, in the subjects of the present study, since there were two main groups with preoperative OEF values near 0.5 and 0.6, respectively, they were studied separately in relation to OEF as an index of the level of imbalance of hemodynamics. It was found that the group with the higher preoperative OEF values (>0.55) has a significantly greater decrease in OEF and showed markedly better improvements in CBF and OEF, postoperatively.

Although there were some cases in each subgroups showing mild improvements in $CMRO_2$ postoperatively, large changes were not observed. This is thought to be due to the fact that the preoperative decreases in CBF were supplemented by the high OEF value, as a results of which $CMRO_2$ was relatively well-preserved; 2.84±0.32 ml/100g/min in ICA lesion and 3.03±30.70 ml.100g/min in the VBA lesion respectively. Since $CMRO_2$ is known to reflect the level of activity of tissues, it is presumed that this must be maintained at a certain level if vascular reconstruction surgery is to be undertaken.

Although negative results were reported about the surgical benefit of bypass procedure for reducing stroke recurrence and stroke death in the international cooperative study,[16,17] it still has been debated.[1,3,8,14,15] In order to prove the effectiveness of vascular reconstruction procedure for cerebral ischemia, meticulous preoperative evaluation is mandatory to differentiate whether the ischemic symptoms are mainly due to the hemodynamic mechanism of major artery occlusion or stenosis, or to the rheological pathology or microcirculatory disturbance in the regions periphery to the major arteries. In the current PET study, however, the relationship between long term prognosis and improvement in hemodynamic mechanism by vascular reconstruction is not well defined yet. In the study of Powers et al.[13] comparing the 21 cases of surgical group and 23 cases of medical group, increased CPP was observed in the surgical group postoperatively, however, protective effect for stroke recurrence was not obtained, they concluded that useful information regarding the stroke recurrence cannot be obtained so far by the measurements of hemodynamics such as PET.

In the present study, there was only a small number of cases in which CBV was simultaneously measured, but it was found that, using only three parameter, CBF, OEF and $CMRO_2$, good preoperative evaluation could be obtained. This is thought to be due to the facts that: 1) the preoperative OEF was higher in comparison with values obtained by others, 2) in all cases of STA-MCA bypass the anastomosis was to the proximal MCA,[4] and 3) in addition to the simple increase in CBF through bypass, there was the possible involvement of brain stem functions influencing cerebral hemodynamics in the cases of VBA lesions.

In the present study, it was found that for cases with markedly unbalanced cerebral hemodynamics, as indicated by low CBF and high OEF, it is possible to prevent the continued deterioration in brain functions by means of surgical vascular reconstruction. PET examination is thought to be an effective means for making the diagnosis for such therapy.

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Table 1. Summary of patients underwent surgical revascularization.

case 1	67M	mCST	Lt IC stenosis	TEA
case 2	46M	TIA	Lt IC stenosis	STA-MCA anastomosis
case 3	68M	TIA	Rt IC occlusion	
case 4	61M	RIND	Lt IC occlusion	
case 5	67M	mCST	Rt IC occlusion	
case 6	51M	VBI	BA stenosis	STA-SCA anastomosis
case 7	57M	mCST	BA stenosis	
case 8	55M	mCST	BA stenosis	
case 9	61M	mCST	Blt VA occlusion	
case 10	58M	mCST	Blt VA stenosis	
case 11	62M	mCST	Blt VA stenosis	VA trans-position
case 12	65 F	mCST	Blt VA stenosis	

mCST: minor completed stroke, TIA: transient ischemic attack, RIND: reversible ischemic neurological deficit, VBI: vertebrobasilar insufficiency, IC: internal carotid artery, BA: basilar artery, VA: vertebral artery, TEA: thromboendarterectomy, STA: superficial temporal artery, MCA: middle cerebral artery, SCA: superior cerebellar artery

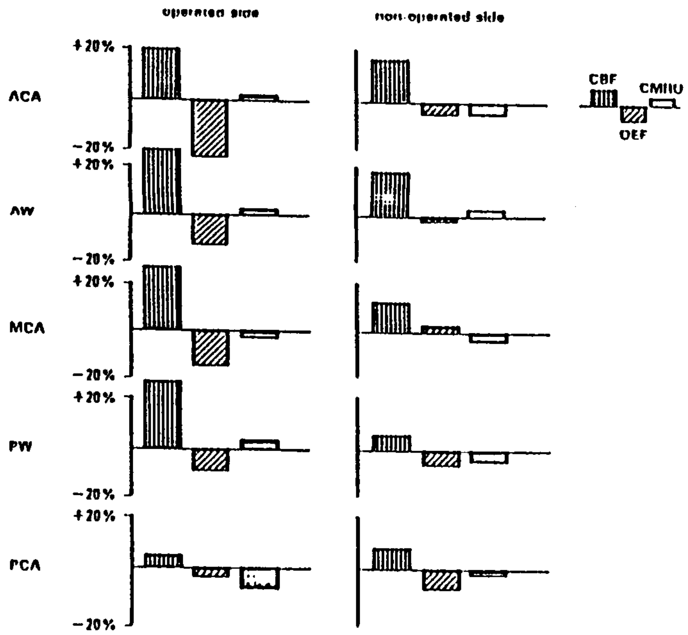

Fig. 1. Postoperative changes of CBF, OEF and $CMRO_2$ in carotid lesion. All parameters were compared with preoperative data in percentage. Increase in CBF and decrease in OEF were observed in operated side and the area of contralateral anterior cerebral artery.
ACA: anterior cerebral artery, AW: anterior watershed area, MCA: middle cerebral artery, PW: posterior watershed area, PCA: posterior cerebral artery

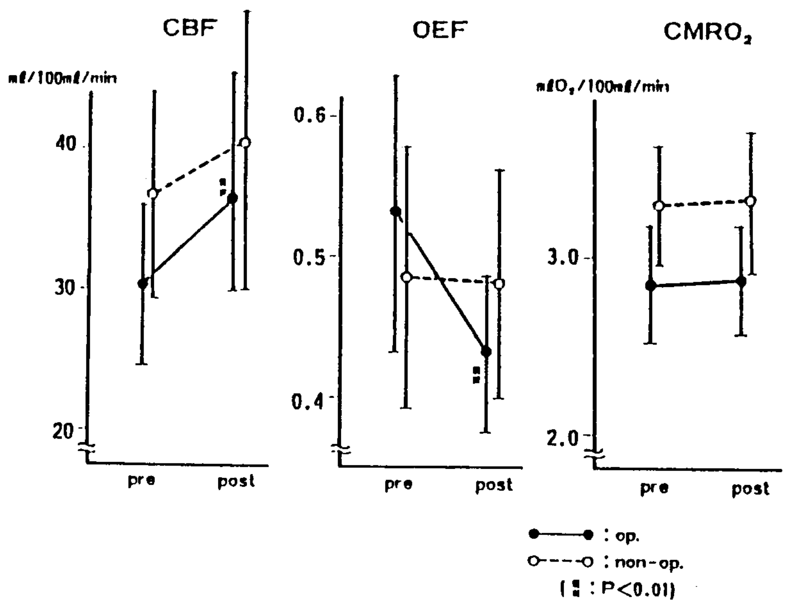

Fig. 2. Pre- and post-operative CBF, OEF and $CMRO_2$ in carotid lesion. Marked increase in CBF ($p<0.01$) and decrease in OEF ($p<0.01$) were observed in the operated side.
op.: operated side, non-op.: contralateral side

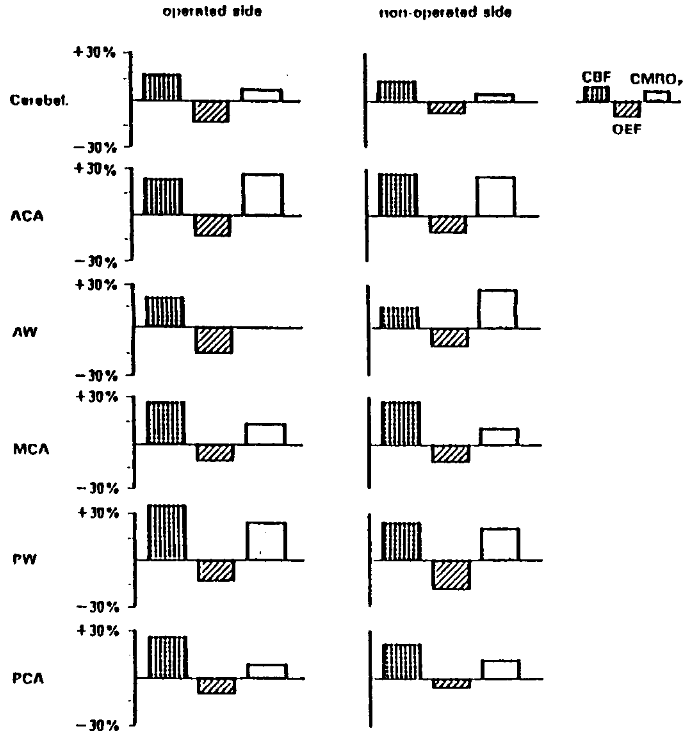

Fig.3. Post operative changes of CBF, OEF and $CMRO_2$ in vertebrobasilar lesion. All parameters were expressed in percentage changes in comparison to the preoperative values. Increase in CBF and decrease in OEF were observed not only in cerebellum but also in cerebral cortex.

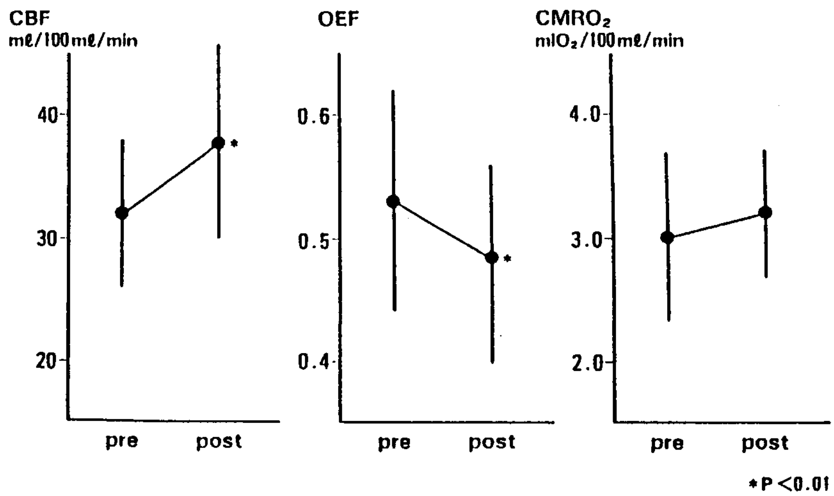

Fig. 4. Pre- and post-operative CBF, OEF and $CMRO_2$ of cerebellum in vertebro-basilar lesion. Marked increase in CBF ($p<0.01$) and decrease in OEF ($p<0.01$) were observed. $CMRO_2$ showed nonsignificant trend of increasing.

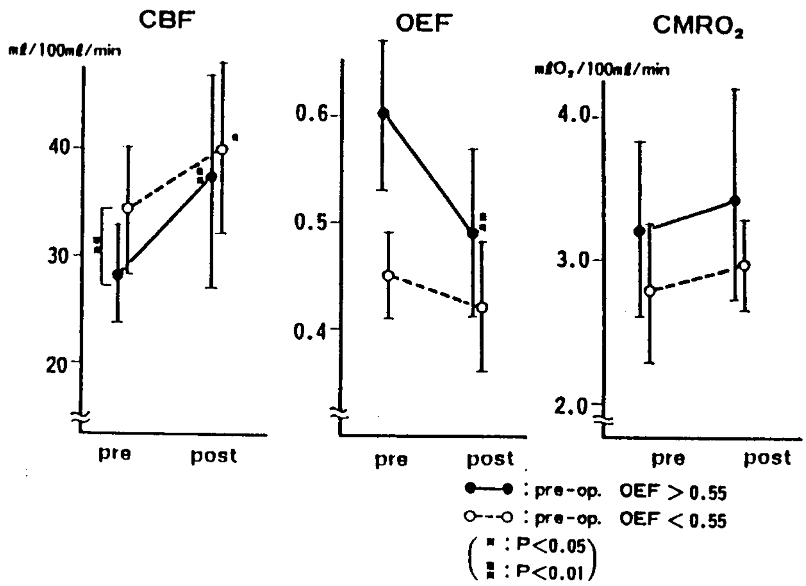

Fig. 5. Correlation between preoperative OEF and postoperative changes. In higher OEF (>0.55), preoperative CBF were significantly reduced (p<0.01), and there were significant improvement in postoperative CBF and OEF (p<0.01).